

## REMARKS

### **I. Status of the Application**

While the Examiner states in the Office Action Summary (page 1 of paper no. 7) that Claims 27-46 are pending, Applicants note that Claims 26-46 are actually pending in the Application. Claim 26 was said to be pending in the previous Amendment and Response to Office Action dated April 24, 2002 and has not been withdrawn in any subsequent papers. Accordingly, Applicants kindly request that the Examiner note that Claims 26-46 are pending in the Application.

Claims 26, 45 and 46 have been amended to recite an aperture instead of an outlet. Support for this amendment is found at page 11, lines 15-18, which states, "The bioreactor vessel should have an aperture to avoid increasing the internal pressure and to allow the natural release of carbon dioxide gas out of the calcifying solution."

Claims 27-32, 35-40 and 41-46 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over US 6,087,003 ("Benoit"). Claims 33-34 stand rejected as being obvious over Benoit in view of US 4,166,536 ("Roberts"). Claim 29 stands rejected as being obvious over Benoit in view of Roberts and US 5,055,272 ("Wheeler"). Claims 33, 42 and 46 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse all rejections in view of the following remarks and the amendments presented herein.

### **II. Claims 27-32, 35-40 and 41-46 are Nonobvious over Benoit**

Claims 27-32, 35-40 and 41-46 stand rejected under § 103(a) as being unpatentable over Benoit. Applicants respectfully traverse this rejection.

Applicants believe that the Examiner has failed to support a *prima facie* case of

obviousness because no reference of record teaches or suggests all the limitations of Claim 26. Claim 26, as amended, describes a device for coating an implant comprising a vessel, a heating element, a support, a stirrer, an inlet, an aperture and a source of carbon dioxide. Benoit fails to teach or suggest an aperture configured to avoid increasing internal pressure of the reactor vessel as is now claimed. In contrast, Benoit teaches at column 5, lines 50-56 coating methods using high-pressure, e.g. 70 – 250 bars. Further, all 25 examples of Benoit teach reaction conditions being at least 110 bar. It is noted that the aperture of the present Application is distinguished from the valve of Benoit in that the aperture is not a switchable mechanism providing for the build-up of pressure during use of the reactor, as is the valve of Benoit. Benoit does not teach or suggest the aperture of Claims 26, 45 and 46 since Benoit requires the valve to be capable of generating significant pressures during use of the reaction.

Also, Benoit does not teach or suggest an implant support. Applicants disclose on page 11, lines 1-3 in the Application, “The implants like hip stems or acetabular cups and the like are held [held] by special hooks fixed on the head-plate of the bioreactor.” In fact, the Examiner even admitted on page 2 of the Office Action (paper no. 7) that Benoit does not teach the implant support required by Claim 26. Thus, the sole reference relied upon to reject Claim 26 fails to teach or suggest all of its claim limitations.

On page 2 of the Office Action (paper no. 7), the Examiner asserts that it would have been obvious to modify the device of Benoit by providing a support for the implant since it is conventional to operatively connect to the reactor vessel a support for an article being treated. However, nowhere does Benoit suggest this modification. In fact, not one of the 25 Examples of Benoit suggests the use of support for the article being treated. Only applicants' disclosure provides this teaching and the Examiner cannot use hindsight reconstruction to arrive at

applicants' claimed subject matter.

Applicants respectfully disagree with the Examiner's comments at the top of page 3 in the previous Office Action (paper no. 7) that it would have been obvious to use the Benoit apparatus to coat a variety of materials including those particulate materials to be used as an implant since it is said to be known to implant pharmaceutical compositions. The mere fact that Benoit *can* be modified cannot render Claim 26 obvious without a motivation for the modification. The Examiner, however, has not cited the source for the motivation to use the device of Benoit to coat the materials of interest in the present Application. Benoit merely refers to coating organic and inorganic compounds used in pharmaceutical compositions, agrochemical compositions, etc. at column 6, lines 34-56. Each of the 25 Examples in Benoit teaches that the substance to be coated is in the form of a free flowing powder, which presumably does not require any support. Benoit certainly provides no disclosure that such a support would be advantageous.

Because Claim 26 is nonobvious in light of Benoit, it follows that all claims directly or indirectly dependent therefrom, namely Claims 27-44, are also nonobvious for the reasons mentioned herein above. Further, because Claims 45 and 46 delineate the same claim elements which are neither taught nor suggested by Benoit (e.g. an implant support), it follows that Claims 45 and 46 cannot be found obvious solely in light of Benoit because of the same reasoning as that relating to Claim 26. Accordingly, it follows that the obviousness rejection of all pending claims made solely in light of Benoit (i.e. Claims 27-28, 30-32 and 35-46) is deemed overcome.

Claims 27-28 are said to be obvious in light of Benoit. Claims 27-28 are nonobvious by virtue of their dependency, either directly or indirectly, from Claim 26 for the reasons presented above relating to Claim 26. Claim 28 is nonobvious for the additional reason that Claim 28

exemplifies unexpected results. Indeed, achieving successful results using a spinning speed of 100 RPM is a surprising unexpected result. When referring to coating solid particles, Benoit teaches at column 9, lines 60-65, "Agitation speeds can normally vary between 200 and 400 RPM." Further, of the 25 examples presented by Benoit, the least amount of agitation is 210 RPM (see Example 20), which is more than twice the amount of agitation claimed in Claim 28. Thus, Benoit does not teach or suggest using agitation speeds less than 200 RPM. Accordingly, there is no suggestion to use an agitation speed less than 200 RPM. Therefore, Applicants submit that Claim 28 is patentable for this additional reason.

Claims 30-31 stand rejected as being obvious over Benoit. The Examiner asserts that it would be obvious to use the solenoid or electro-valve described in Claim 31 in the apparatus of Benoit. Claims 30-31 are nonobvious by virtue of their dependency, either directly or indirectly, from Claim 26 for the reasons presented above relating to Claim 26. Applicants further believe that Claims 30-31 are nonobvious for the additional reason that there is no motivation to a person of ordinary skill to substitute a standard valve with a solenoid or electro-valve because there is no reason to believe from Benoit that a standard valve is inadequate for this particular application. Thus, Applicants submit that Claims 30-31 are not obvious in this aspect as well.

Claims 35-36 stand rejected as being obvious over Benoit because Benoit teaches the use of a 1.5 L autoclave. Claims 35-36 are nonobvious by virtue of their direct dependency from Claim 26 for the reasons presented above relating to Claim 26. Further, there are no cited references of record, which suggest to a person of ordinary skill to modify Benoit to employ a reactor vessel having a capacity other than 1.5 L. Thus, Applicants deem this rejection to be overcome for this additional reason as well.

Claims 37 and 39 stand rejected as being obvious over Benoit. Claims 37-39 are

nonobvious by virtue of their direct dependency from Claim 26 for the reasons presented above relating to Claim 26. Thus, Claims 37 and 39 are deemed nonobvious.

Claim 38 stands rejected as being obvious over the teaching of Benoit at column 11, lines 13-25. Claim 38 is nonobvious by virtue of its direct dependency from Claim 26 for the reasons presented above relating to Claim 26. Applicants respectfully traverse this rejection for the additional reason that the cited reference merely describes a heat exchanger for heating; Benoit does not teach or suggest a thermo-circulator capable of heating and cooling as described by Applicants. (See page 10, lines 35-36 of the Application.) Since the Examiner has made no reference of record teaching or suggesting this claim limitation, Applicants deem this rejection overcome for this additional reason.

Claims 41 and 42 stand rejected as being obvious over Benoit. Claims 41-42 are nonobvious by virtue of their dependency, either directly or indirectly, from Claim 26 for the reasons presented above relating to Claim 26. Applicants respectfully traverse this rejection for the additional reason that the Examiner is applying an improper “obvious to try” rationale. Benoit merely provides guidance as to there being an advantage of controlling temperature and pressure. The guidance of Benoit, however, stops there; it does not teach or suggest using automation. While it is arguably “obvious to try” to control temperature and pressure via an automated system, it is an improper basis for an obvious rejection. Thus, Applicants deem Claims 41 and 42 to be nonobvious for this additional reason.

Claims 43-44 stand rejected as being obvious over Benoit. Claims 43-44 are nonobvious by virtue of their dependency, either directly or indirectly, from Claim 26 for the reasons presented above relating to Claim 26. Applicants traverse this rejection for the additional reason that the Examiner is providing an improper obvious to try rationale. The Examiner states that it

would have been obvious to provide a filter membrane cell and optimize the pore size of the membrane cell. Applicants believe, however, that the Examiner is utilizing an improper “obvious to try” rationale. Benoit provides no indication as to which parameters are critical and no direction as to which of many possible choices is likely to be successful. Benoit merely mentions at column 11, line 53 that the apparatus is equipped with a filtering device. Thus, for this reason and those discussed herein above, Applicants deem Claims 43 and 44 nonobvious.

Claim 32 stands rejected as being obvious over Benoit. Claim 32 is nonobvious by virtue of its direct dependency from Claim 26 for the reasons presented above relating to Claim 26. Applicants respectfully traverse this rejection for the additional reason that Benoit fails to teach or suggest equipping the apparatus with an electrode. Further, Benoit does not suggest that one would even be concerned with the pH within the reactor. Thus, because Benoit fails to teach or suggest all of its claim limitations, Applicants deem Claim 32 nonobvious.

Claim 45 stands rejected as being obvious over Benoit. Applicants respectfully traverse this rejection. Applicants renew the above comments relating to Claim 26, 27, 30, 32 and 39. Because Benoit does not teach or suggest all of the limitations of Claim 45 (e.g. an implant support or an aperture) and no other reference of record remedies this deficiency, Applicants deem Claim 45 patentable.

Claim 46 stands rejected as being obvious over Benoit. Applicants respectfully traverse this rejection. The above comments relating to Claims 26, 41 and 45 apply here and are incorporated by reference. Because Benoit does not teach or suggest all of the limitations of Claim 46 (e.g. an implant support or an aperture) and no other reference of record remedies this deficiency, Applicants deem Claim 46 patentable.

Claim 29 stands rejected over Benoit. Claim 29 is nonobvious by virtue of its direct

dependency from Claim 26 for the reasons presented above relating to Claim 26. Claim 29 is nonobvious for the additional reason that Benoit fails to teach or suggest a porous sparger. The Examiner makes this admission at the bottom of page 5 of the Office Action (paper no. 7). Thus, Applicants deem Claim 29 nonobvious.

### **III. Claims 33-34 are Not Obvious over Benoit in view of Roberts**

Claims 33-34 stand rejected as being obvious over Benoit in view of Roberts. Applicants respectfully traverse this rejection.

Claims 33-34 are nonobvious by virtue of their direct dependency from Claim 26 for the reasons presented above relating to Claim 26. Namely, Benoit does not teach or suggest an implant support or an aperture. Neither Roberts nor any other reference of record cures this deficiency.

In addition, Applicants believe that the combination of Benoit and Roberts is improper because there is no motivation to combine these references. Because Roberts is concerned with protecting a metallic vessel from corrosive chemicals (i.e. chemicals that are highly acidic or basic) whereas Claims 33 and 34 are concerned with preventing deposits of carbonated calcium phosphate (a relatively innocuous compound), the nature of the problem to be solved is not similar enough to motivate the combination of references. Further, neither reference suggests that a coating made of, for example polytetrafluoroethylene, would be suitable for preventing deposits of carbonated calcium phosphate on a surface. Thus, Claims 33 and 34 are not obvious for the additional reason that the combination of references is improper.

**IV. Claim 29 is Not Obvious over Benoit in view of Roberts and Wheeler**

Claim 29, which is dependent from Claim 26, stands rejected as being obvious over Benoit in view of Roberts and Wheeler. Applicants respectfully traverse this rejection.

As discussed above, Claim 29 is nonobvious because Benoit fails to teach or suggest a porous sparger, an implant support and an aperture. Roberts and Wheeler do not correct these deficiencies of Benoit by teaching an implant support or an aperture. Thus, the present rejection is deemed overcome because there are no references of record that teach or suggest all of the limitations of Claim 29.

**V. Claims 33, 42 and 46 are Definite pursuant to 35 U.S.C. § 112 ¶2**

Claims 33, 42 and 46 stand rejected under § 112, second paragraph as being indefinite. The Examiner states on page 6 of the Office Action that Claim 33 is vague and indefinite because Applicants' device for coating an implant is silent as to the presence of any composition that might form a calcium phosphate coating. Further, the rejection of Claims 42 and 46 are rejected for vagueness because of similar reasoning. Applicants respectfully traverse this rejection for each claim.

The definiteness of claim language employed must be analyzed, not in a vacuum, but always in light of the teachings of the prior art and of the particular application. Definiteness of a claim is an objective requirement as determined by a person of ordinary skill in the art.

Applicants note that Claim 26, the independent claim from which Claims 33 and 42 depend, as well as Claim 46 are directed towards a device for coating an implant. The specification of the present Application describes methods for applying the apparatus of Claim 26. These methods include using compositions that might form a calcium phosphate coating.

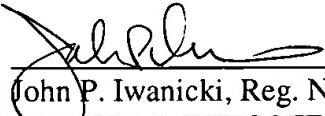
(See page 6, lines 15-20 of the Application.). Moreover, the specification states on page 10, lines 22-27 that the bioactive carbonated calcium phosphate coatings on implants are produced in the described bioreactor. Example 1 in the Application provides further insight as to the source of a calcium phosphate coating. Applicants respectfully submit that a person of ordinary skill in the art reading the claims in light of the specification would be able to determine the context for which the claimed device is to be applied. Thus, when Claims 33, 42 and 46 are interpreted in light of the specification and not in a vacuum, Applicants believe that the cited claims are definite and are in condition for allowance.

## VI. Conclusion

Having addressed all outstanding issues, Applicants respectfully request reconsideration and allowance of all pending claims (Claims 26-46). To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims:**

Kindly amend the claims as follows:

26. (Twice Amended) A device for coating an implant comprising:

- (a) a reactor vessel;
- (b) a heating element operatively connected to the reactor vessel;
- (c) an implant support operatively connected to the reactor vessel;
- (d) a stirrer disposed within the reactor vessel;
- (f) an inlet and [outlet] an aperture operatively connected to the reactor vessel;
- (g) a controlled source of carbon dioxide operatively connected to the inlet, [and]

wherein the [outlet] aperture is configured to avoid increasing internal pressure of the reactor vessel.

45. (Amended) A device for coating an implant comprising:

- (a) a reactor vessel;
- (b) a heating element capable of maintaining a temperature between 5 and 50 °C, operatively connected to the reactor vessel;
- (c) an implant support operatively connected to the reactor vessel;
- (d) a stirrer disposed within the reactor vessel, which is magnetically coupled to a stirring system;
- (e) an electrode to measure pH operatively connected to the reactor vessel;
- (f) an inlet operatively connected to the reactor vessel and operatively connected to a valve to control the flow of carbon dioxide;
- (g) a source of carbon dioxide operatively connected to the valve to control the flow of carbon dioxide; and
- (h) an [outlet] aperture operatively connected to the reactor vessel, wherein the [outlet] aperture is configured to avoid increasing internal pressure of the reactor vessel.



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46. (Amended) A device for coating an implant comprising:
- (a) a reactor vessel;
  - (b) a heating element capable of maintaining a temperature between 5 and 50 °C, operatively connected to the reactor vessel;
  - (c) an implant support operatively connected to the reactor vessel;
  - (d) a stirrer disposed within the reactor vessel, which is magnetically coupled to a stirring system;
  - (e) an electrode to measure pH operatively connected to the reactor vessel;
  - (f) an inlet operatively connected to the reactor vessel and operatively connected to a valve to control the flow of carbon dioxide;
  - (g) a source of carbon dioxide operatively connected to the valve to control the flow of carbon dioxide;
  - (h) an [outlet] aperture operatively connected to the reactor vessel, wherein the [outlet] aperture is configured to avoid increasing internal pressure of the reactor vessel; and
  - (i) an automated system to measure, record and/or control parameters selected from the group consisting of pH, temperature, carbon dioxide flow, calcium concentration, phosphate concentration, and carbonate concentration.